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PATENT SPECIFICATION

746.016



Date of Application and filing Complete Specification: June 24, 1952.
No. 27388/54.

Application made in United States of America on Oct. 1, 1951.

Application made in United States of America on Oct. 1, 1951.
(Divided out of No. 745,900).

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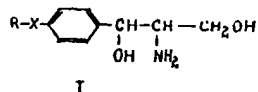
COMPLETE SPECIFICATION

Amino Diol Compounds and method for preparing same

We, STERLING DRUG INC., a corporation organised under the laws of the State of Delaware, United States of America, of 1450 Broadway, New York, State of New York, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to new chemical compounds and the preparation thereof, said compounds being useful as intermediates for the production of other chemical compounds as hereinafter described.

More particularly, this invention relates to new compounds having the formula

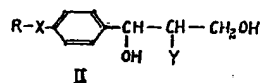


where R is a hydrocarbon radical having 1—7 carbon atoms, and X is S or SO₂. The hydrocarbon radical R includes aliphatic, cycloaliphatic, aryl, and benzyl radicals having 1—7 carbon atoms and represents, for example: branched and unbranched alkyl radicals, such as methyl, ethyl, n-propyl, n-butyl, isobutyl, n-heptyl, isoamyl; alkenyl radicals, such as allyl, methallyl; cycloalkyl radicals, such as cyclohexyl, cyclopentyl; benzyl; phenyl; and ortho-, meta- and para-tolyl radicals.

This application is a divisional of Appln. 15864/52 (Serial No. 745,900) and types of compounds embraced by the generic formula hereinabove are set out in that application.

The amines of the present invention are prepared by deacylating the 2-(aliphatic carboxylic acylamino)-1-(4-hydrocarbonylmercapto- (or sulfonyl) phenyl)-1,3-propanediols of the aforesaid parent application. The latter compounds (having the formula II below) are

readily deacylated by treatment with hot mineral acids to yield the corresponding free amines having the formula I above,



where R and X have the same significance as in formula I above and Y is an aliphatic carboxylic acylamino radical.

These novel amines I are readily acylated to yield acylamino derivatives and if desired can be readily reconverted to the aliphatic carboxylic acylamino derivatives II. The amines I react with organic and inorganic acids to form salts. When the acylamino compounds of Appln. 15864/52 (Serial No. 745,900) wherein the acylamino group is other than acetyl amino are desired, it is generally advantageous to prepare them by acylating the appropriate 2-amino-1-(4-hydrocarbonylmercaptophenyl)-1,3-propanediol of the present invention which has been obtained by hydrolysis of the corresponding 2-acetyl amino-1-(4-hydrocarbonylmercaptophenyl)-1,3-propanediol. This is described in the aforesaid application.

Moreover the 2-amino-1-(4-hydrocarbonylmercaptophenyl)-1,3-propanediols of the present invention are utilizable as intermediates in the production of the 2-amino-1-(4-hydrocarbonylsulfonylphenyl)-1,3-propanediols.

It will be appreciated that in preparing the 2-aliphatic carboxylic acylamino-1-(4-hydrocarbonylmercaptophenyl)-1,3-propanediols of the aforesaid parent application using racemic or optically inactive intermediates, the final products will of course be obtained in a racemic or optically inactive form. When it is desired to obtain the optically active forms of the acylaminodiols, we have found that it is generally most convenient to acylate the appropriate optically active 2-amino-1-(4-hydro-

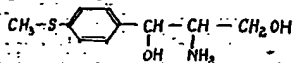
5 ester as set forth in the parent application.

10 employed as the starting material in the oxida-

EXAMPLE 1.

35. 2-Amino-1-(4-methylmercaptophenyl)-1,3-propanediol.

40 concentrated hydrochloric acid, and 500 parts by



A solution of 17.5 g. of the 2-amino-1-(4-

or optically inactive form of the compound,

the methanolic filtrate being retained for treatment. 65

solved in 50 ml. of water and the resulting 85

151° C.; obtained by benzylation of *d*-threon- 100

g. of sodium chloride was dissolved in this. 120

washed with a little saturated aqueous sodium chloride solution and dried at 70° C. There was thus obtained 15.0 g. of crude levo-rotary 2-amino-1-(4-methylmercaptophenyl)-1,3-propanediol which melted at 147—150° C. This product was recrystallized from 150 ml. of methanol to yield 11.9 g. of the pure levo-rotary amine which melted at 151—153° C. By concentrating the mother liquor, 3.0 g. of solid consisting largely of the racemic amine was recovered.

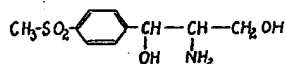
The filtrate (A) retained as indicated above was evaporated at reduced pressure. The residue thus obtained was dissolved in 100 ml. of water containing 62 ml. of concentrated hydrochloric acid and the solution was made alkaline by addition of 13 ml. of 35% aqueous sodium hydroxide solution. 20 g. of sodium chloride was dissolved in this solution which was then cooled to 5° C. The heavy crop of crystalline solid which separated from the solution was collected on a filter, washed with a few ml. of saturated aqueous sodium chloride solution and dried at 70° C. There was thus obtained 13.5 g. of crude dextro-rotary 2-amino-1-(4-methylmercaptophenyl)-1,3-propanediol. This product was recrystallized from methanol to yield 8.5 g. of the pure dextro-rotary amine which melted at 151—153° C. By concentrating the mother liquor, 5.0 g. of solid consisting largely of the racemic amine was recovered.

EXAMPLE 2.

2-Amino-1-(4-methylsulfonylphenyl)-1,3-propanediol.

A mixture of 5 g. of the dextro-rotary 2-dichloroacetyl-amino-1-(4-methylsulfonylphenyl)-1,3-propanediol, 9 ml. of concentrated hydrochloric acid, and 40 ml. of water was heated on a steam bath for one hour. The water was removed from the resulting solution by distillation *in vacuo* to give a light yellow residual syrup which solidified on standing at room temperature (*circa* 25° C.) for several days. This solid was heated to 60—70° C. with 20 ml. of saturated aqueous sodium chloride solution until all dissolved. The resulting solution was treated with 3.5 ml. of 35% aqueous sodium hydroxide solution and extracted while still warm with approximately 100 ml. of n-butanol. On cooling and stand-

ing, 0.9 g. of white crystals separated from the butanol extract. This product, which was levo-rotary 2-amino-1-(4-methylsulfonylphenyl)-1,3-propane-diol, having the formula



melted at 141.4—142.6° C. and had $[\alpha]_D^{25} = -19.8^\circ$ (1% solution in 95% ethanol). This water-soluble base formed a water-soluble hydrochloride which melted at 200.4—202.6° C. and had $[\alpha]_D^{25} = -26.0^\circ$ (1% solution in 95% alcohol).

In analogous fashion, when the levo-rotary and the racemic 2-dichloroacetyl-amino-1-(4-methylsulfonylphenyl)-1,3-propanediols are deacylated by treatment with concentrated hydrochloric acid, there are obtained the dextro-rotary and the racemic 2-amino-1-(4-methylsulfonylphenyl)-1,3-propanediols, respectively.

It is to be understood that all acylamino-diols and aminodiols referred to throughout the specification are threo forms.

What we claim is:—

1. A process for preparing threo amino diol compounds of the formula I herein, which comprises deacylating a threo compound of the formula II herein.

2. A process according to claim 1, in which the compound of formula II is treated with a hot mineral acid.

3. A process according to claim 1 or 2, in which R in the formulæ is alkyl, e.g. methyl.

4. The processes of preparing threo amino diol compounds of the formula I herein, substantially as set forth in the Examples.

5. Threo amino diol compounds of the formula I herein, whenever prepared by a process according to any one of the preceding claims.

6. A threo amino diol compound of the formula I herein.

7. A compound according to claim 6, in which R in the formula is alkyl, e.g. methyl.

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Aminodiol compounds and method for preparing same

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IPC Classification:
EC Classification:
Equivalents:

Abstract

The invention comprises threo aminodiol compounds of the general formula (wherein R represents a hydrocarbon radical of 1-7 carbon atoms and X represents S or SO₂), and the preparation thereof by deacylating their N-acyl derivatives (the acyl group being the residue of an aliphatic carboxylic acid), e.g. by treatment with hot mineral acid. The products form salts with organic and inorganic acids, and their racemic forms may be resolved into optically active forms by means of optically active organic acids. In examples (1) dl-threo-2 - acetylamino - 1 - (p - methylmercaptophenyl) - 1:3 - propanediol is heated with dilute hydrochloric acid, and the resulting dlthreo - 2 - amino - 1 - (p - methylmercaptophenyl) - 1:3 - propanediol is resolved with the aid of d - tartaric acid or d - N - benzoylthreonine; (2) (+) -, (-) - or racemic - threo-2 - dichloroacetylamino - 1 - (p - methylsulphonylphenyl) - 1:3 - propanediol is hydrolysed as in (1) to (-) -, (+) - or racemicthreo - 2 - amino - 1 - (p - methylsulphonylphenyl)-1:3-propanediol.

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